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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,988	09/22/2003	Patrick L. Iversen	50450-8060	1777

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
09/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,988	IVERSEN ET AL.	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Amendment/Response dated 6/9/08

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Porter et al (USPN 6,245,747 hereafter '747) in view of Unger et al (USPN 5,542,935 hereafter '935). The claims are drawn to method of delivering a therapeutic agent to a tumor site comprising administering parenterally a microbubble composition comprising a chemotherapeutic compound, and where the agent is release without the use of external stimulation.

4. The '747 patent discloses a method of applying a coated microbubble formulation to tumor site (abstract). The microbubble is coated with a protein such as human serum albumin (col. 4, lin. 57-65), and range in size from 0.1-10 microns (col. 4, lin. 23-26). The microbubbles

are filled with a perfluorocarbon gas such as perfluorobutane (col. 4, lin. 35-40). The microbubbles can carry a wide variety of active agents including analgesics, antibiotics and chemotherapeutic compounds (col. 6, lin. 60-col. 7, lin. 19), where the compounds are delivered to specific locations such as specific tumor sites (col. 7, lin. 60-65). The reference is however silent to the specific chemotherapeutic compounds of the instant claims. These compounds are well known in the art as can be seen in the '935 patent. Also the method of the '747 calls for an external energy source to rupture the microbubbles upon delivery. This however is not a requirement for all delivery methods as shown in the '935 patent.

5. The '935 patent teaches suspension of perfluorocarbon filled, protein coated microbubbles (abstract). The microbubbles are coated with human serum albumin (col. 22, lin. 50-63). The perfluorocarbon gases include perfluoromethane, perfluoropropane and perfluoropentane (col. 17, lin. 17-23). The microbubbles are used to delivery active agents such as taxol and doxorubicin (col. 24, lin. 27-40). The microbubbles are useful in various diagnostic and therapeutic methods such as the treatment of tumors since the microbubbles accumulate near diseased tissue (col. 23, lin. 61-col. 24, lin. 15). The microbubbles are delivered parenterally to the diseased site into the body cavity (col. 32, lin. 29-43). The microbubbles measure in size from 30-100 nanometers (col. 31, lin. 5-15). The nanoparticles are delivered to the body where the microparticles where the drugs can be delivered with or without an ultrasonic external energy source (col. 34, lin. 39-50). It would have been obvious to include the compounds of the '935 patent into the method of the '747 in order to treat a wide variety of tumor sites.

6. With these things in mind, it would have been obvious to follow the suggestions of the '747 patent to include chemotherapeutic compounds into the treatment method in order to treat

the specific tumor sites disclosed in the method. It would have been obvious to avoid the external energy application as disclosed in the '935 patent in order to provide a more timely and cost effective method. Further skipping the step would obviously provide a more efficient method when applying the method to the treatment of lung tumors. It would have been obvious to combine the teachings and suggestions of the art with an expected result of an efficient and cost effective treatment for lung cancer.

Response to Arguments

Applicant's arguments filed 6/9/08 have been fully considered but they are not persuasive. Applicant argues that:

> The combination of the Porter and Unger patents teaches away from the current invention and requires an external energy source not required by the instant invention

Regarding this argument it remains the position of the Examiner that the combination of the Porter and Unger patents continue to obviate the instant claims. First, the Porter patent discloses a microbubble formulation in a liquid composition where the microbubbles are coated and stabilized with a filmogenic protein coating (col. 4, lin. 58-60). The filmogenic protein coating includes albumin and the occasional polysaccharide (col. 4, lin. 60-col. 5, lin. 1-10). The microbubbles have a diameter from 0.1-10 microns (col. 6, lin. 40-46). The formulation is delivered parenterally via bolus injection and can be applied to any system in the body (col. 8, lin. 1-18). These disclosures meet each of the limitations of claims 19 and 24. The reference discloses various active agents yet is silent to the specific chemotactic agents of the instant claims. The Unger patent provides these chemotactic agents combined into a microbubble

formulation. Applicant argues that Unger discloses lipid micro spheres and that they would not be compatible with the microbubbles of the Porter patent. Applicant also argues that Unger teaches away from albumin coating of these micro spheres. These arguments are irrelevant since Unger is only relied upon for establishing the knowledge in the art of combining specific chemotactic agents into microbubble formulations. Applicant argues that Unger teaches away from the use of albumin since it would form brittle micro spheres that are easily broken due to pressure changes, such as when they are applied to the heart or lung. However in situations when an exterior ultrasound device is not required or recommended these albumin containing micro spheres would be useful. See col. 34, lin. 39-50 where microspehre4s are applied and drugs are release without the use of ultrasonic devices. The Unger patent acknowledges the use of albumin as a useful stabilizer when the micro spheres are required to break and rupture in specific areas, areas identical to those of the Porter patent such ad the heart and lungs. Unger is a secondary reference only relied upon for specific teachings. Where the micro spheres are coated with same proteins of the Porter patent bares no weight since the patent is used to establish the level of skill regarding chemotactic agents and microbubbles. With these things in mind it would be obvious to combine the chemotactic agents of the Unger into the albumin coated microbubbles of the Porter patent to arrive at a stable perfluorobutane filled microbubble encapsulated with a filmogenic fluid.

For these reasons the claims remain obviated.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 7:00-4:30; every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618